

IN THE SPECIFICATION:

Please replace the paragraphs appearing on page 25 with the following rewritten paragraphs:

Characterization of beta-sheet mutant 12A

B¹ Expression of the fusion protein Mu 12A-minor coat protein 3 on the surface of the recombinant phages and expression of Mu 12A in *E. coli* strain HB 2151 were detected by means of Western-blot analyses using the anti-G3P and anti-E-Tag antibodies (Pharmacia-Biotech), respectively. The DNA sequences of mutant 12A in phagemid pGCKT 8-3 and of gamma-II-crystalline wild-type are depicted in Fig. 7. The DNA sequence starts at the Sfi I cleavage site which is already present in the starting phagemid pCANTAB 5E and ends, in the case of pGCKT 8-3, at the Bst EII site newly introduced into the gamma II-crystalline gene and, in the case of the gamma II-crystalline wild-type gene, at the original sequence. Fig. 8 depicts the amino acid sequences derived therefrom (Mu 12A; SEQ ID NO: 19). Codon randomization at amino acid position 36 does not change the amino acid arginine at this position. Computer modelling modeling of mutant 12A shows that the amino acid exchanges do not cause large alterations in the protein structure compared with the starting protein. However, the net charge becomes more positive.

Expression of Mu 12A in pET-20b

In order to characterize mutant 12A in detail, the DNA was recloned into plasmid pET-20b (Novagen). The plasmid makes possible a high expression of the recombinant DNA in *E. coli* strain BL 21 and simple purification of the foreign proteins. Genes are expressed here without signal peptide and with a C terminal fusion of 6 histidine residues. The DNAs of mutant 12A and of gamma II-crystalline wild-type were amplified by means of PCR using the appropriate phagemid phagemid DNA and primers GC 20bback12A/GC for 20b for mutant 12A and GC 20bbackWT/GC for 20b for the wild-type (Fig. 9). The PCR fragments were cleaved with restriction endonucleases Nde I and Bam HI and cloned into vector pET 20b cut with Nde I/ Bam HI. Fig. 10 depicts the theoretical amino acid sequence of mutant 12 A (Mu 12A-HIS; SEQ ID NO: 21) and of gamma II-crystalline, respectively, after expression in pET 20b. The first 10 N terminal amino acids of mutant 12 A were confirmed by N terminal protein sequencing.

IN THE CLAIMS:

1. (Currently Amended) Protein with beta-sheet structure, wherein amino acids exposed on the a surface in of at least two β -strands exposed on the a surface of at least one beta sheet exposed on the a surface of the protein are specifically substituted, deleted or inserted, mutagenized, wherein the mutagenizing is selected from the group consisting of an insertion, a deletion, a substitution, and combinations thereof, such that the protein has a new property, wherein the new property is selected from the group consisting of an specific antigen binding properties specificity, or a new catalytic activity, and of a new fluorescence properties property.

2. (Currently Amended) Protein according to Claim 1, wherein it is included in the protein to be mutagenized is selected from the group consisting of a crystallines, a spherulines, a heat shock proteins, a cold shock proteins, a β -helix proteins, a lipocalins, a serpins, a fibronectins, a or transcription factors, a or is green fluorescent protein (GFP), a nerve growth factor (NGF), a tendamistat, and a or lysozyme.

3. (Currently Amended) Protein according to Claim 1, wherein, amino acids exposed on the surface in of three beta strands exposed on the surface are substituted, deleted or inserted of the protein are mutagenized.

4. (Currently Amended) Protein according to Claim 1, wherein, amino acids exposed on the surface in of at least four or more beta strands exposed on the surface are substituted, deleted or inserted mutagenized.

5. (Currently Amended) Protein according to claim 1, wherein amino acids exposed on the surface in of at least two beta strands in of at least two beta sheets are substituted, deleted or inserted mutagenized.

6. (Currently Amended) Protein according to claim 1, wherein, amino acids exposed on the surface in of three beta strands in of two antiparallel beta sheets are substituted, deleted or inserted mutagenized.

7. (Currently Amended) Protein according to claim 1, wherein it the protein is a vertebrate crystalline, of vertebrates, preferably rodents, birds or fish.

8. (Currently Amended) Protein according to claim 1, wherein, it is an alpha, beta or gamma-crystalline the protein is selected from the group consisting of an alpha-crystalline, a beta-crystalline, and a gamma-crystalline.

9. (Currently Amended) Protein according to claim 1, wherein, it the protein is a gamma-II-crystalline protein.

10. (Currently Amended) Protein according to claim 1, wherein an amino acids exposed on the surface of the protein ~~are substituted, deleted or inserted~~ is mutagenized in a region of the beta sheet that is accessible to a solvent ~~or to a binding partner~~.

11. (Currently Amended) Protein according to claim 1, wherein, an amino acids exposed on the surface ~~are~~ is mutagenized ~~substituted, deleted or inserted~~ in a region of the protein selected from the group consisting of a β -sheet structure of a domain ~~or of the protein and a β -sheet structure of a subunit of the protein~~.

12. (Currently Amended) Protein according to claim 4 9, wherein, ~~it is a gamma-II crystalline which has been obtained by substitution, deletion or insertion of one or more of the~~ at least one of the amino acids Lys 2, Thr 4, Tyr 6, Cys 15, Glu 17, Ser 19, Arg 36 and Asp 38 ~~in~~ of a bovine gamma-II-crystalline is mutagenized.

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cont

13. (Currently Amended) Protein according to claim 1, wherein, an amino acids exposed on the surface of the protein ~~have been substituted, deleted or inserted~~ is mutagenized in the beta sheet such that ~~it~~ the protein has a new property, wherein the new property is selected from the group consisting of an antibody-like binding properties or an enzymic (catalytic) antigen binding specificity and a catalytic activity.

14. (Currently Amended) Protein according to Claim 42 13, wherein ~~it has the new property is an antigen binding specificity for a compound selected from the group consisting of~~ estradiol ~~or the conjugate thereof, and~~ BSA- β -estradiol-17-hemisuccinate.

15. (Currently Amended) Protein according to claim 1, wherein, ~~it~~ the protein has binding specificity for a compound selected from the group consisting of estradiol ~~or the conjugate thereof, and~~ BSA- β -estradiol-17-hemisuccinate, and wherein the protein has the an amino acid sequence comprising one of SEQ ID NO-19: 19 and ~~or~~ SEQ ID NO-24: 21.

16. (Currently Amended) Protein A composition comprising a protein according to claim 1, ~~wherein, it is combined with~~ and at least one other proteins or non-protein substances.

17. (Previously Amended) DNA coding for a protein according to claim 1.

18. (Original) RNA derived from the DNA according to claim 17.

19. (Currently Cancelled)

20. (Currently Amended) Method for preparing a the protein according to of claim 1, the method comprising the following steps:

- (a) ~~Mutagenesis of the~~ mutagenizing a DNA coding for a protein with beta-sheet structure in those regions which code for at least two beta strands, exposed on the surface, of a beta sheet exposed on the surface;
- (b) ~~Expression of the mutants~~ expressing the DNA obtained in step (a) in a suitable an expression system to produce a protein encoded by the expressed DNA; and
- (c) ~~Selection and isolation of mutants having the desired binding properties and/or the desired catalytic activity; optionally~~ selecting a protein encoded by the expressed DNA having a desired property; and
- (d) ~~Expression and purification of the beta sheet mutated proteins~~ isolating the protein encoded by the expressed DNA having the desired property.

21. (Currently Amended) Method according to Claim 20, wherein the ~~mutagenesis~~ mutagenizing comprises a site-specific substitution, ~~deletion or insertion of specific amino acid positions (site-specific mutagenesis) or non-specific amino acid positions (random mutagenesis)~~ in the beta sheet.

22. (Currently Amended) Method according to claim 20, wherein, ~~the mutants in step b) are expressed in~~ the expressing is in a system selected from the group consisting of a prokaryotic cell, or a eukaryotic cells, in and a cell-free system as a complex with ribosomes or on the surface of plant or animal cells, yeast cells or phages, viruses or bacteria.

23. (Currently Amended) Method according to claim 20, wherein ~~mutants further comprising identifying a protein having the a desired binding properties are selected~~ property by contacting these mutants the protein with the a binding partner, wherein the binding of the protein to the binding partner identifies the protein as having the desired property and isolating those mutants having the desired binding affinity.

24. (Currently Amended) Method according to claim 20, wherein ~~mutants having the desired~~ the desired property of the protein is a catalytic activity and wherein identifying the protein having a desired catalytic activity comprises ~~properties are selected by contacting these mutants~~ the protein encoded by the expressed DNA with their a substrate, wherein the binding of the protein encoded by the expressed DNA to the substrate identifies the protein encoded by the expressed DNA as and isolating these mutants having the desired catalytic activity.

25. (Currently Amended) ~~Use of a protein according to claim 1, A method of preparing a composition for use in an application selected from the group consisting of diagnostics, and therapy, in cosmetics, bioseparation, and biosensors, and reduction of and reducing harmful substances, the method comprising:~~

(a) providing a protein according to claim 1; and

(b) preparing a composition for use in an application selected from the group consisting of diagnostics, therapy, cosmetics, bioseparation, biosensors, and reducing harmful substances by incorporating therein the protein according to claim 1.

26. (New) Protein according to claim 7, wherein the vertebrate is selected from the group consisting of a rodent, a bird, and a fish.

27. (New) Protein according to claim 1, wherein an amino acid exposed on the surface of the protein is mutagenized in a region of the beta sheet that is accessible to a binding partner.

28. (New) Protein according to claim 1, wherein an amino acid exposed on the surface is mutagenized in a β -sheet structure of a subunit of the protein.

29. (New) The method of claim 20, further comprising purifying the protein encoded by the expressed DNA.

30. (New) The method of claim 20, wherein the expressing is on the surface of an entity selected from the group consisting of a plant cell, an animal cell, a yeast cell, a virus, and a bacterium.

31. (New) The method according to Claim 20, wherein the mutagenizing comprises a site-specific deletion in the beta sheet.

32. (New) The method according to Claim 20, wherein the mutagenizing comprises a site-specific insertion in the beta sheet.

33. (New) The method according to Claim 20, wherein the mutagenizing comprises a random substitution in the beta sheet.

34. (New) The method according to Claim 20, wherein the mutagenizing comprises a random deletion in the beta sheet.

35. (New) The method according to Claim 20, wherein the mutagenizing comprises a random insertion in the beta sheet.

36. (New) A vector comprising the DNA of claim 17.

37. (New) The vector of claim 36, wherein the vector is a prokaryotic vector.

38. (New) The vector of claim 36, wherein the vector is a eukaryotic vector.

39. (New) The vector of claim 36, wherein the DNA has a nucleotide sequence that encodes a protein having an amino acid sequence that is one of SEQ ID NO: 19 and SEQ ID NO: 21.

40. (New) A cell comprising the DNA of claim 17.

41. (New) The cell of claim 40, wherein the DNA has a nucleotide sequence that encodes a protein having an amino acid sequence that is one of SEQ ID NO: 19 and SEQ ID NO: 21.

42. (New) A mutagenized gamma crystalline polypeptide, wherein the mutagenizing is selected from the group consisting of an insertion, a deletion, a substitution, and combinations thereof, such that the gamma crystalline polypeptide has a new binding property.

43. (New) A method for preparing a gamma crystalline protein with a new binding property, the method comprising mutagenizing a gamma crystalline polypeptide, wherein the mutagenizing is selected from the group consisting of an insertion, a deletion, a substitution and combinations thereof, to provide a mutagenized gamma crystalline protein with a new binding property.

44. (New) A method of preparing a protein with a new binding property, the method comprising:

- (a) mutagenizing a gamma crystalline protein to provide a gamma crystalline protein with a new binding property; and
- (b) combining the mutagenized gamma crystalline protein with another protein to provide a protein with a new binding property.

45. (New) The method according to claim 44, wherein the mutagenizing is selected from the group consisting of an insertion, a deletion, a substitution and combinations thereof.